## REMARKS

The Office Action of August 4, 2003 presents the examination of claims 6-15, 17, 19, 20, 28, and 29. Claims 1-5, 16, 18, and 21-27 are withdrawn from consideration. Claims 6, 13, and 14 are canceled herein. Non-elected claims 1-5, 18, and 21-27 are also canceled. Claims 7-12, 15-17, 19-20, and 28 are amended. Support for amendments to claims 7, 8, and 28 is found in former claim 6. Support for the recitation of "8 to 14 amino acids in length" recited in claim 9 is found on page 22, lines 4-8 of the specification. Support for "amino acid residue at position 2 and/or the C-terminus is substituted by another amino acid residue" as recited in claims 9, 11, and 12 is found in former claims 13-15. No new matter is inserted into the application.

***Request for Initialed PTO-1449***

On page 2 of the Office Action, the Examiner states that he has acknowledged and considered the Information Disclosure Statements filed on June 1, 2001 and November 4, 2002. However, Applicants have filed three Information Disclosure Statements on June 1, 2001, June 22, 2001, and November 4, 2002. Only the references listed on the form PTO-1449 filed on June 22, 2001 have been initialed by the Examiner and returned to Applicants.

Although returned to Applicants with the Office Action of August 4, 2003, none of the references listed on the form PTO-1449 filed on June 1, 2001 have been initialed. Further, Applicants have not yet received a copy of the form PTO-1449 filed with the IDS of November 4, 2002. Therefore, Applicants respectfully request that the Examiner consider the references contained in the Information Disclosure Statements of June 1, 2001 and November 4, 2002 and initial and return to Applicants copies of the PTO-1449 forms that accompanied those Information Disclosure Statements. Copies of the PTO-1449 forms are attached hereto for the Examiner's convenience.

***Election/Restriction***

The Examiner maintains the restriction requirement such that claims 1-5, 16, 18, and 21-27 are withdrawn from consideration. Non-elected claims 1-5, 18, and 21-27 are canceled, thus rendering the withdrawal thereof moot. Applicants respectfully traverse the withdrawal of claim 16. Reconsideration of the claim and withdrawal of the restriction requirement are respectfully requested.

Specifically, Applicants respectfully request that the Examiner rejoin claim 16 to the examined claims. Claim 16, as amended, is directed to the isolated tumor antigen peptide

derivative of claim 12, which comprises a sequence selected from an amino acid sequence shown in any of SEQ ID NOs: 19-21. SEQ ID NOs: 19, 20, and 21 are variant sequences of SEQ ID NOs: 3, 4, and 5, respectively, wherein the amino acid residue at position 2 and/or the C-terminal amino acid is substituted by another amino acid. The Examiner has already searched for claim 12, which recites SEQ ID NOs: 3-5 and derivatives thereof. Claim 16 further defines claim 12 by limiting the derivatives to SEQ ID NOs: 19-21. Since the Examiner has already searched the scope of claim 12, it would not place an undue burden on the Examiner to include claim 16 (which is dependent from claim 12) in the elected Group II.

For all of these reasons, Applicants respectfully request that the Examiner withdraw the restriction requirement with regard to claim 16, and examine the claim in the present application.

***Claim Objections***

The Examiner objects to claims 17, 19, and 28 for being dependent upon non-elected claims. Claims 17, 19, and 28 are amended to depend from currently examined claims. Thus, the instant objection is overcome.

***Rejection under 35 U.S.C. § 101***

The Examiner rejects claims 6 and 9-15 under 35 U.S.C. § 101 for allegedly being directed to non-statutory subject matter. Claims 6, 13, and 14 are canceled, thus rendering rejection thereof moot. Applicants respectfully traverse the rejection of the pending claims. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

The claims are amended to recite "isolated" as suggested by the Examiner. Thus, the instant rejection is overcome.

***Rejection under 35 U.S.C. § 112, first paragraph***

*Written Description*

The Examiner rejects claims 9-15, 17, 19-20, and 28-29 under 35 U.S.C. § 112, first paragraph for allegedly containing subject matter not described in the specification. Claims 13 and 14 are canceled, thus rendering rejection thereof moot. Applicants respectfully traverse the rejection of the pending claims. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

The Examiner asserts that the specification does not provide adequate written description for "partial peptide" and "derivative(s)." In the amended claims, the phrase "partial

peptide" is deleted. The tumor antigen peptide is defined as a "peptide of 8 to 14 amino acids in length that is a fragment of the amino acid sequence of SEQ ID NO:1." Further, "derivative" is defined as "derivative which comprises an amino acid residue at position 2 and/or the C-terminus substituted by another amino acid residue, and which has the functionally equivalent properties." Applicants respectfully submit that the amendments to the claims obviate the Examiner's rejections.

On page 5 of the Office Action, the Examiner writes, "Applicant is invited to point to clear support or specific examples of the claimed invention in the specification as filed." The Examiner is advised that the tumor antigen peptides of the present invention are described on page 20, line 3 to page 26, line 15. Derivatives thereof are described on page 26, line 16 to page 31, line 19. Pharmaceutical compositions are described on page 31, line 20 to page 33, line 15. Diagnostic agents are described on page 39, line 21 to page 41, line 10.

Further, Example 4 of the specification describes the actual selection of the tumor antigen peptides of 8 to 11 amino acids in length (i.e., SEQ ID NOs: 3-18). Thus, the Examiner's assertion that derivatives are not disclosed is incorrect. Examples 5 to 7 describe the preparation of tumor antigen peptides (i.e., SEQ ID

NOs: 3-5). Examples 8 and 9 instruct the skilled artisan how to determine activity of the tumor antigen peptides according to the present invention.

For these reasons, Applicants respectfully submit that the instant specification contains a written description which fully complies with the requirements of 35 U.S.C. § 112, first paragraph. Withdrawal of the instant rejection is therefore respectfully requested.

*Enablement*

The Examiner rejects claims 7, 8, 17, and 20 under 35 U.S.C. § 112, first paragraph for allegedly containing subject matter not enabled by the specification. Applicants respectfully traverse. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

The Examiner asserts that the specification, while being enabling for a composition comprising tumor antigen proteins for treating cancer cells in vitro, does not reasonably provide enablement for a pharmaceutical composition comprising a tumor antigen protein for preventing cancer cells *in vivo*.

First, the claims as amended are not directed to preventing cancer cells. Thus, this aspect of the Examiner's rejection is

obviated. However, Applicants respectfully disagree with the Examiner's assertion that the present invention is only enabled for a composition comprising tumor antigen proteins for treating cancer cells in vitro.

Specifically, on page 7 of the Office Action, the Examiner writes, "[T]he specification has not taught one of skill in the art how to extrapolate these findings of CTL response into methods of preventing tumors or whether the tumor antigen is effective as an in vivo pharmaceutical composition." Applicants respectfully submit that the present invention is enabled for a composition comprising tumor antigen proteins for treating cancer cells both in vitro and in vivo. As evidence thereof, Applicants submit herewith two journal articles published prior to the priority date of the present application demonstrating that tumor antigens were effective in the clinical setting.

Rosenberg et al. *Nature Medicine*, 4(3):321-327 (1998) (attached hereto as Exhibit 1) demonstrates the successful use of a tumor antigen protein as a cancer vaccine to treat patients with metastatic melanoma. Rosenberg et al. writes, "Synthetic peptide vaccines based on genes encoding cancer antigens hold promise for the development of novel cancer immunotherapies." (See, abstract page 321). Slinghoff et al., *Clinical Cancer Research*, 7:3012-3024

(2001) (attached hereto as Exhibit 2) demonstrates the successful phase I trial of the $gp100_{280-288}$ tumor antigen peptide in treating patients with melanoma. These publications clearly show that pharmaceutical compositions comprising tumor antigen peptides (such as those of the present invention) can be used in vivo.

For all of the above reasons, Applicants respectfully submit that the instant claims are fully enabled by the specification such that the requirements of 35 U.S.C. § 112, first paragraph are met. Withdrawal of the instant rejection is therefore respectfully requested.

***Rejection under 35 U.S.C. § 102***

*Nagase et al.*

The Examiner rejects claims 6, 9, and 11-15 under 35 U.S.C. § 102(b) for allegedly being anticipated by Nagase et al. (*DNA Research*, 5(5):277-286, 1998). Claims 6, 13, and 14 are canceled, thus rendering rejection thereof moot. Applicants respectfully traverse the rejection of the pending claims. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

Independent claim 9, as amended, is directed to an isolated tumor antigen peptide of 8 to 14 amino acids in length that is a

fragment of the amino acid sequence of SEQ ID NO:1, and that binds to an HLA antigen and is recognized by CTLs, or a derivative thereof which comprises an amino acid residue at position 2 and/or the C-terminus substituted by another amino acid residue, and which has the functionally equivalent properties. Nagase et al. fails to anticipate the instant claim 9. Specially, Nagase et al. fails to describe any peptide of 8 to 14 amino acids in length. Further, Nagase et al. merely determined the base sequence of clones obtained from a human brain cDNA library. Nagase et al. fails to describe either the function or the activity of the clone having the base sequence. Since Nagase et al. fails to describe each and every element of claim 9, Nagase fails to anticipate the claim.

Claim 12, as amended, is directed to the isolated tumor antigen peptide of claim 11, which comprises a sequence selected from an amino acid sequence shown in any one of SEQ ID NOs:3-5, or a derivative thereof which comprises a sequence selected from an amino acid sequence shown in any one of SEQ ID NOs:3-5 wherein the amino acid residue at position 2 and/or the C-terminus is substituted by another amino acid residue and which has the functionally equivalent properties. The Examiner asserts that Nagase et al. teaches a protein of SEQ ID NO:5 in which the second amino acid is tyrosine. Applicants respectfully disagree. SEQ ID

NO:5 is only 8 amino acids in length (Leu Tyr Gln Ala Val Ala Thr Ile). Nagase et al. does not describe any peptide having such a small number of amino acids. Further, Nagase et al. fails to recognize that this small peptide has the function of being a tumor antigen peptide.

For all of the above reasons, Applicants respectfully submit that Nagase et al. fails to anticipate the present invention. Withdrawal of the instant rejection is therefore respectfully requested.

*Sette '954*

The Examiner rejects claims 6-15, 17, 19-20 and 28-29 under 35 U.S.C. § 102(a) for allegedly being anticipated by Sette '954 (WO 99/45954). Claims 6, 13, and 14 are canceled, thus rendering rejection thereof moot. Applicants respectfully traverse the rejection of the pending claims. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

The Examiner asserts that Sette '954 discloses a peptide sequence which is a partial match of SEQ ID NO:5. Although the 9mer in Sette '954 partially overlaps with the sequence of SEQ ID NO:5, the sequences are different from one another in the amino acid residue at position 3. The present invention includes

derivatives of SEQ ID NO:5; however, the claims directed to these derivatives specify that that such derivatives comprise amino acid substitutions at position 2 and/or the C-terminus, rather than at position 3 of the specifically described peptides. Accordingly, the instant claims do not encompass the 9mer described in Sette '954.

Further, Sette '954 merely describes a general approach to motifs for HLA-A24.1 and theoretical peptides, which have not been actually demonstrated to have any activity. In contrast, the peptides claimed in the present application are demonstrated to be tumor antigen peptides.

For all of the above reasons, Applicants respectfully submit that Sette '954 fails to anticipate the present invention. Withdrawal of the instant rejection is therefore respectfully requested.

***Conclusion***

Applicants respectfully submit that the above amendments and/or remarks fully address and overcome and/or render moot the objections/rejections of record. The present application is in condition for allowance. The Examiner is respectfully requested to

issue a Notice of Allowance indicating that claims 7-12, 15-17, 19-20, and 28-29 are allowed.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Kristi L. Rupert, Ph.D. (Reg. No. 45,702) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

Pursuant to the provisions of 37 C.F.R. §§ 1.17 and 1.136(a), the Applicants hereby petition for an extension of three (3) months to February 4, 2004, in which to file a reply to the Office Action. The required fee of $950.00 is enclosed herewith.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees

required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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Attachments:
(1) Exhibit 1: Rosenberg et al. *Nature Medicine*, 4(3):321-327 (1998)
(2) Exhibit 2: Slinghoff et al., Clinical Cancer Research, 7:3012-3024 (2001)
(3) Form PTO-1449 from IDS filed on June 1, 2001
(4) Form PTO-1449 from IDS filed on November 4, 2002